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Acute inflammatory responses to Stachybotrys chartarum in the lungs of infant rats: time course and possible mechanisms

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Abstract

Stachybotrys chartarum has been linked to building-related respiratory problems including pulmonary hemorrhage in infants. The macrocyclic trichothecenes produced by S. chartarum have been the primary focus of many investigations. However, in addition to trichothecenes this fungus is capable of producing other secondary metabolites and a number of protein factors. This study examines the effects of intact, autoclaved, and ethanol-extracted spores on the lungs of infant rats as an approach to differentiate between secondary metabolites and protein factors. Seven-day-old infant rats were exposed intratracheally to 1 x 10(5) spores/g body weight (toxic strain JS58-17) and sacrificed at various times up to 72 h. The inflammatory response was measured by morphometric analysis of the lungs and determination of inflammatory cells and cytokine concentrations in bronchoalveolar lavage (BAL) fluid. Alveolar space was greatly reduced in animals exposed to fungal spores compared to phosphate buffered saline (PBS)-treated controls. The largest effects were observed in pups treated with intact spores where alveolar space 24 h after treatment was 42.1% compared to 56.8% for autoclaved spores, 51.1% for ethanol-extracted spores, and 60.6% for PBS-treated controls. The effects of different spore preparations on inflammatory cells, cytokine, and protein concentrations in the BAL fluid can be ranked as intact > autoclaved > extracted. Tumor necrosis factor alfa (TNF-alpha), interleukin 1-beta (IL-1beta), and neutrophils were the most sensitive indicators of inflammation. The difference between autoclaved (100% trichothecene toxicity, denatured/enzymatically inactive proteins) and intact (100% trichothecene activity, unaltered/released proteins) spores indicates the involvement of fungal proteins in the inflammatory response to S. chartarum and sheds new light on the clinical importance of "nontoxic" strains.

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